REMARKS

Applicants thank Examiners Shin and Angell for the opportunity to discuss the pending rejections with Applicants' representatives in the telephone interview conducted January 29, 2008, a summary of which is attached.

Claims 1 and 18 are currently amended to clarify the claims. Support for these claim amendments is found throughout the specification as filed, for example at Example 17, beginning on page 94. Accordingly, no new matter is introduced by these amendments.

35 U.S.C. § 102(a) - Anticipation

Claims 1 and 9-16 are rejected under 35 U.S.C. § 102(a) as being anticipated by the cited PR Newswire reference. The Examiner asserts that "PR Newswire teaches a method of treating ulcerative colitis/pouchitis in a patient comprising administering ISIS 2302. ...Accordingly, all limitations set forth in the claims are taught by PR Newswire." *Office Action* at 3.

Applicants note that independent claims 1 and 18 recite "a composition suitable for rectal use." The Examiner has acknowledged that "PR Newswire does not teach that the ISIS 2302 compound is formulated for rectal use." *Office Action* at 4. Nor is this feature inherent in the disclosure of PR Newswire. Because PR Newswire does not disclose each and every element of claims 1 and 18, or the claims dependent therefrom, either expressly or inherently, it cannot anticipate any of the pending claims. Applicants therefore request that the Examiner reconsider and withdraw the rejection of the pending claims under 35 U.S.C. § 102(a) as anticipated by PR Newswire.

35 U.S.C. § 103(a) – Obviousness

Claims 1-3 and 7-24 are rejected as being unpatentable over PR Newswire as applied to claims 1 and 9-16 in the 35 U.S.C. § 102(a) rejection, and further in view of Bennett *et al.* (U.S. 6,111,094). The Examiner argues that "PR Newswire teaches a method of treating ulcerative colitis/pouchitis in a patient comprising administering ISIS 2302. ...PR Newswire does not teach that the ISIS 2302 compound is formulated for rectal use." *Office Action* at 4. The Examiner asserts that it would have been obvious to "modify the method of treating UC/pouchitis of PR Newswire by formulating the ISIS 2302 compound for rectal use in enemas

or suppositories further comprising a penetration enhancer as taught by Bennett et al." *Id.* Applicants respectfully traverse.

The well-established "Stempel Doctrine" stands for the proposition that a patent applicant can effectively swear back of and remove a cited prior art reference by showing that he or she made that portion of the claimed invention that is disclosed in the prior art reference. (*In re Stempel*, 113 U.S.P.Q. 77 (CCPA 1957)). In other words, a patent applicant need not demonstrate that he or she made the entire claimed invention in order to remove a cited prior art reference. The applicant need only demonstrate prior possession of that portion of the claimed invention that is disclosed in the prior art reference and nothing more. In the instant case, the Examiner asserts that PR Newswire discloses "a method of treating ulcerative colitis/pouchitis in a patient comprising administering ISIS 2302. ...PR Newswire does not teach that the ISIS 2302 compound is formulated for rectal use."

Without acquiescing to the Examiner's assertions regarding what PR Newswire discloses, and without conceding that the Examiner has established a prima facie case of obviousness, Applicants submit herewith an inventors' declaration pursuant to 37 C.F.R. § 1.131 (attached as Exhibit A). The declaration establishes that Applicants were in possession of as much of the claimed invention as is allegedly disclosed in the PR Newswire reference prior to February 11, 2003.

Specifically, paragraphs 3-4 of the declaration state:

> The above-referenced application claims priority to U.S. Provisional Patent Application Serial No. 60/447215, which was filed on February 13, 2003. Example 17 of the 60/447215 application beginning on page 91 is entitled "Treatment of pouchitis with ISIS-2302 [] enema formulation." This example describes the results of a 6 week study using ISIS 2302 to treat patients with pouchitis. All of the events and activities described in Example 17 were performed in the United States by one or both of us personally, or by others at the direction of one or both of us.
>
> This evidence clearly establishes that at least six weeks prior to the filing of the 60/447215 application, we possessed as much of the claimed invention as is allegedly disclosed in the PR Newswire reference. Because the 60/447215 application was filed two days after the date listed on the PR Newswire reference, this evidence establishes that we possessed as much of the claimed invention as is allegedly disclosed in the PR Newswire reference prior to February 11, 2003.

Example 17 of the 60/447215 application describes a six week clinical trial of administering ISIS 2302 to treat pouchitis, as well as the results of the clinical trial. This shows that Applicants possessed the results of the trial at the time of filing of the '215 application, and possessed the protocol for the clinical trial at least six weeks before the filing of the '215 application – one cannot begin a clinical trial without possessing at least the basics of the trial protocol at the start of the trial. Thus, Applicants possessed the basic clinical protocol of treating pouchitis in a patient by administering ISIS 2302 by at least January 2, 2003, which is six weeks before the February 13, 2003 filing date of the '215 application. Because the PR Newswire reference does not disclose any results of a clinical trial, Applicants do not need to show that they possessed the results of the clinical trial prior to the publication of PR Newswire. Therefore, the declaration and accompanying evidence demonstrate that by January 2, 2003, Applicants possessed as much of the claimed invention as is allegedly disclosed in the PR Newswire reference on its ostensible publication date of February 11, 2003. As a result, the PR Newswire reference is not available as prior art.

Because the PR Newswire reference is not available as prior art, the Examiner's arguments under 35 U.S.C. § 103(a) do not establish a prima facie case of obviousness. Applicants therefore request that the Examiner reconsider and withdraw the rejection of the pending claims under 35 U.S.C. § 103(a) as unpatentable over PR Newswire in view of Bennett *et al.*

Double Patenting Rejection over U.S. Patent 6,169,079

Claims 1-3 and 7-24 are rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 2-3 of U.S. Patent No. 6,169,079 ("the '079 patent") in view of PR Newswire. The Examiner argues that "[b]oth instant claims and reference claims are drawn to treating an inflammatory disease by administering an antisense pharmaceutical composition comprising ISIS 2302, which decreases the expression/activity of ICAM-1." *Office Action* at 6. The Examiner acknowledges that the reference claims do not recite treating pouchitis, but argues that it would be obvious to modify the reference claims based on the PR Newswire reference:

> Although the reference claims do not recite treatment of pouchitis *per se*, it would have been obvious to one of ordinary skill in the art to use the methods in the

> reference claims to treat pouchitis with a reasonable expectation of success, because PR Newswire taught that ISIS 2303 was already undergoing Phase II trials for treatment of pouchitis/ulcerative colitis as of the earliest filing date sought in the instant application. *Office Action* at 7.

Applicants respectfully traverse.

As explained above in responding to the 35 U.S.C. § 103(a) rejection of the claims over the PR Newswire reference, the rule 1.131 declaration submitted herewith establishes that Applicants possessed as much of the claimed invention as is allegedly disclosed in the PR Newswire reference prior to its publication, and therefore it is not available as prior art. As the Examiner notes, "the reference claims do not recite treatment of pouchitis *per se*," and in the absence of the alleged disclosure of the PR Newswire reference, the Examiner has failed to establish a prima facie case of obviousness of the claimed invention over claims 2-3 of the 6,169,079 patent.

In addition, as Applicants have noted in previous responses, the M.P.E.P. and caselaw are unambiguous in stating that the specification of a cited patent may not be considered in making an obviousness-type double-patenting rejection:

> When considering whether the invention defined in a claim of an application would have been an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art. *General Foods Corp. v. Studiengesellschaft Kohle mbH*, 972 F.2d 1272, 1279, 23 USPQ2d 1839, 1846 (Fed. Cir. 1992). This does not mean that one is precluded from all use of the patent disclosure. *M.P.E.P. §804 II.B.1* (emphasis added).

According to the M.P.E.P., the disclosure of a patent cited for obviousness-type double-patenting can be considered for only two limited reasons. The first is to learn the meaning of a term in the patent claim, in which case the specification is used as a dictionary. *See Toro Co. v. White Consol. Indus., Inc.*, 199 F.3d 1295, 1299, 53 USPQ2d 1065, 1067 (Fed. Cir. 1999). The second is to determine what is claimed by looking to an embodiment of the invention disclosed in the specification. This is done to assist the Examiner in determining what is claimed. *See In re Vogel*, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970).

Neither of these exceptions apply to the instant case. The Examiner's argument that "the specification of 6,169,079 B1 expressly states, 'ISIS 2302 ... was the most active of the series'" is not using the specification of the '079 patent to define a claim term or to better understand the

scope of the claims. *See Office Action* at 6 (emphasis added). Instead, the Examiner is relying on the teachings of the '079 patent to provide a basis for one of skill in the art to select the species of SEQ ID NO:1 from all of the species of antisense molecules that fall within the scope of claims 2-3 of the '079 patent. According to the M.P.E.P., this is impermissible, as the claims of the instant application must be obvious over the claims of the '079 patent, not the entire disclosure of the '079 patent.

Applicants clarify for the record that in any past or present responses or proceedings arguing that the M.P.E.P. and caselaw state that the "the disclosure of the patent may not be used as prior art," Applicants are not asserting that a particular cited patent is not available as prior art under any statute. Rather, Applicants are arguing that when cited as a double-patenting reference, the M.P.E.P. and cases cited therein state that the disclosure of the cited patent cannot be considered in making the double-patenting rejection, except for the limited reasons discussed above.

In sum, the Examiner's obviousness-type double-patenting rejection fails because it depends on the PR Newswire reference which is not available as prior art, and because the M.P.E.P. states that the Examiner may not rely on the disclosure of the '079 patent to provide a basis to select the species of SEQ ID NO:1. Therefore, Applicants respectfully request that the obviousness-type double-patenting rejection of claims 1-3 and 7-24 over U.S. Patent No. 6,169,079 be withdrawn.

Double Patenting Rejections over U.S. Patent 6,096,722

The Examiner also rejects claims 1-3 and 7-24 on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 7-11, 16-17, and 19 of U.S. Patent No. 6,096,722 ("the '722 patent") in view of PR Newswire. To support the rejection, the Examiner makes the following argument:

> The reference claims are drawn to a method of treating an inflammatory disease comprising administering ISIS 2302 formulated in a penetration enhancer, wherein the inflammatory disease is ulcerative colitis. ...Although the reference claims do not recite treatment of pouchitis *per se*, it would have been obvious to one of ordinary skill in the art to use the methods in the reference claims to treat pouchitis with a reasonable expectation of success, because PR Newswire taught that ISIS 2302 was already undergoing Phase II trials for treatment of

pouchitis/ulcerative colitis as of the earliest filing date sought in the instant application. *Office Action* at 7 (emphasis added).

As noted above in the response to the 35 U.S.C. § 103(a) rejection of the pending claims over PR Newswire, Applicants have submitted a rule 1.131 declaration which establishes that the PR Newswire reference is not available as prior art. The Examiner has admitted that the reference claims do not disclose treating pouchitis. In the absence of the alleged disclosure in the PR Newswire reference that ISIS 2302 can be used to treat pouchitis, the Examiner has failed to establish a prima facie case of obviousness over claims 7-11, 16-17, and 19 of U.S. Patent No. 6,096,722. Applicants therefore respectfully request the withdrawal of the obviousness-type double-patenting rejection of the pending claims over U.S. Patent No. 6,096,722.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, the Applicants are not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. The Applicants reserve the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that the Applicants have made any disclaimers or disavowals of any subject matter supported by the present application.

Patents and Applications

Applicant wishes to draw the Examiner's attention to the following patents or applications of the present application's assignee. Applicants encourage the Examiner to review and monitor the prosecution of the following patents and/or applications throughout the pendency of this application.

Patent / Serial Number	Title	Issued / Filed
10/793,497	COMPOSITIONS AND METHODS FOR NON-PARENTAL DELIVERY OF OLIGONUCLEOTIDES	03.04.2004
6,747,014	COMPOSITIONS AND METHODS FOR NON-PARENTAL DELIVERY OF OLIGONUCLEOTIDES	06.08.2004
09/315,298	COMPOSITIONS AND METHODS FOR NON-PARENTAL DELIVERY OF OLIGONUCLEOTIDES	05.20.1999
11/237,063	COMPOSITIONS AND METHODS FOR NON-PARENTAL DELIVERY OF OLIGONUCLEOTIDES	09.28.2005
6,169,079	OLIGONUCLEOTIDE INHIBITION OF CELL ADHESION	01.02.2001
6,300,491	OLIGONUCLEOTIDE INHIBITION OF CELL ADHESION	10.09.2001
09/659,288	OLIGONUCLEOTIDE MODULATION OF CELL ADHESION	09.12.2000
6,093,811	OLIGONUCLEOTIDE MODULATION OF CELL ADHESION	07.25.2000
6,015,894	OLIGONUCLEOTIDE MODULATION OF CELL ADHESION	01.18.2000
5,843,738	OLIGONUCLEOTIDE MODULATION OF CELL ADHESION	12.01.1998
6,096,722	ANTISENSE MODULATION OF CELL ADHESION MOLECULE EXPRESSION AND TREATMENT OF CELL ADHESION MOLECULE-ASSOCIATED DISEASES	08.01.2000
6,111,094	ENHANCED ANTISENSE MODULATION OF ICAM-1	08.29.2000
10/454,663	OLIGONUCLEOTIDE MODULATION OF CELL ADHESION	06.04.2003
6,849,612	OLIGONUCLEOTIDE MODULATION OF CELL ADHESION	02.01.2005
6,887,906	COMPOSITIONS AND METHODS FOR THE DELIVERY OF OLIGONUCLEOTIDES VIA THE ALIMENTARY CANAL	05.03.2005

08/886,829	COMPOSITIONS AND METHODS FOR THE DELIVERY OF OLIGONUCLEOTIDES VIA THE ALIMENTARY CANAL	07.01.1997
07/939,855	OLIGONUCLEOTIDE MODULATION OF CELL ADHESION	09.02.1992
5,843,738	OLIGONUCLEOTIDE MODULATION OF CELL ADHESION	12.01.1998
5,591,623	OLIGONUCLEOTIDE MODULATION OF CELL ADHESION	01.07.1997
5,514,788	OLIGONUCLEOTIDE MODULATION OF CELL ADHESION	05.07.1996
5,883,082	COMPOSITIONS AND METHODS FOR PREVENTING AND TREATING ALLOGRAFT REJECTION	03.16.1999
07/567,286	OLIGONUCLEOTIDE MODULATION OF CELL ADHESION	08.14.1990
09/082,624	COMPOSITIONS AND METHODS FOR NON-PARENTAL DELIVERY OF OLIGONUCLEOTIDES	05.21.1998

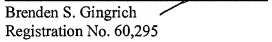
Conclusion

Applicants submit that the present application is in condition for allowance and respectfully requests an action to that effect. If any issues remain, the Examiner is invited to contact Applicants' counsel at the number provided below in order to resolve such issues promptly. Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 2/28/08

By: 

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